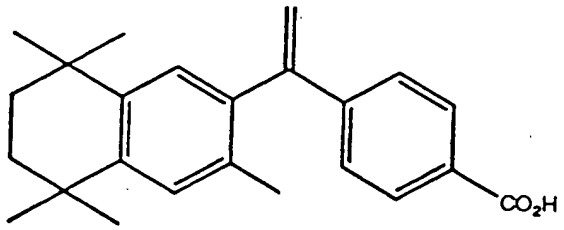
48. A compound having the formula:



Please cancel claim 38 without prejudice.

REMARKS

In the Office Action mailed February 24, 1997, claims 33-44 were rejected under 35 USC § 112 (par 2), stating in particular that the term "ligand" is overly broad and indefinite. While applicants do not agree tht the term "ligand" is overly broad and indefinite, and respectfully traverse this basis for rejection, nevertheless to advance prosecution of this application, applicants have made amendments to these claims as follows. The term "ligand" in composition claims 33-37, and also in method claims 39-46, has been amended to the term "compound". In addition, method claims 39-46 have been amended to now incorporate and specify the specific processes (i.e., disease states) modulated by the claimed methods of using the specified compounds. In particular, claim 40 has been rewritten in independent form and includes the limitations of prior claim 38 upon which it was formerly dependent. Claim 38 has accordingly been cancelled without prejudice. Claim 40 has also been amended to specify that said first and second compounds are

separately present, and to specify said activated intracellular receptor as forming a dimer with said activated Retinoid X Receptor. This amendment further clarifies and defines the invention and is discussed in the specification at, e.g., pp. 67, 84, and 89-96. Claims 39 and 41-44 have been rewritten to now be dependent on amended claim 40 (rather than on now-cancelled claim 38). Claims 33-34, 36-37, 39-40, and 42-44 have also been amended to utilize the singular rather than the plural for a receptor activated by the compounds.

Based on the above amendments, applicants believe that claims 33-37 and 39-44 are now in condition for allowance.

Further, applicants respectfully traverse the rejection under § 112 that the term "ligand" is overly broad and indefinite. Claims 33-37, 39-44, and 47 are directed to the disclosed compositions, and to methods for using them, comprising the combination of two different ligands (compounds) -- a first ligand which selectively activates Retinoid X Receptors (RXRs) in preference to Retinoic Acid Receptors (RARs), and a second ligand having the reverse properties of selectively activating RARs in preference to RXRs. The specification discloses such ligands and provides clear guidance on how to predictably select and assay such ligands to verify their claimed activity.

For example, at page 3, line 29 to page 4, line 1 of the specification, the compound all-trans-retinoic acid is identified as a ligand upon which the transcription-modulating activity of Retinoic Acid Receptor-alpha (RAR-alpha) depends. At page 4, lines

8-14, all-trans-retinoic acid is stated to be a natural ligand for RARs and capable of binding those receptors with high affinity, resulting in the regulation of gene expression. At page 5, lines 19-24, the compound 9-cis-retinoic acid is described as a natural endogenous ligand for Retinoid X Receptors (RXRs), able to bind and transactivate the RXRs as well as RARs, and therefore a bifunctional ligand. At pages 73-75 of the specification, compounds including 3-Methyl-TTNCB and 3-Methyl-TTNEB, among others, are disclosed which preferentially activate Retinoid X Receptors versus Retinoic Acid Receptors. Further, pp. 67-72 of the specification describes the co-transfection assay which can be used to evaluate retinoid receptor subtype selectivity of a ligand. The specification also discloses the surprising and greater than additive effect of combining these two different types of ligands together. See, for example, pp. 89-96 of the specification. Accordingly, applicants respectfully submit that the term "ligand" in this application is not overly broad and indefinite.

New dependent claim 47 has been added by this amendment, and specifies that said first and second compounds are administered as a single composition. Support for claim 47 is found at, e.g., pp. 89-96 of the specification and originally filed claims 33 and 36.

New claim 48 has also been added with this Amendment. Support for the compound designated in the specification as 3-methyl-TTNEB, and also as 4-[1-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-napthyl)ethenyl] benzoic acid, is found in numerous

places in the specification. For example, the formula is given on p. 3, and the representative structure is given on p. 16. (This compound is also specified in pending claim 7 of co-pending application Serial No. 08/141,496.)

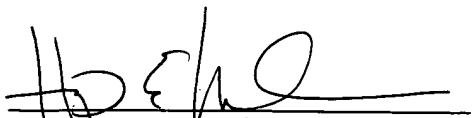
Based on the above amendments and remarks, applicants believe this application and its claims 33-37 and 39-48 are now in condition for allowance. Reconsideration and allowance of the claims is respectfully requested.

Accompanying this Response and Amendment is a petition requesting a three-month extension of time to file this Response and Amendment, along with our check in the amount of $930.00 for the extension fee. (The period for response is thereby extended to August 25, 1997 since the six-month date of August 24, 1997 falls on a Sunday.)

The Assistant Commissioner is hereby authorized to charge any additional fees which may be required by this communication, or credit any overpayment, to Deposit Account No. 12-2475.

Respectfully submitted,

LYON & LYON LLP

Dated: August 25, 1997 By: 

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